Antiretroviral therapy in Thai adults and children with HIV-1 infection
Ananworanich, J.

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Chapter 14:
Creation of a drug fund for post-clinical trial access to antiretrovirals

Creation of a drug fund for post-clinical trial access to antiretrovirals

Jintanat Ananworanich, Thechini Cheunyam, Songsaeng Teranatchalerm, Mark A Boyce, Kat Runyantham, Joep Lange, David Cooper,
Prapaph Phanuphak

The long running debate about clinical trial sponsors’ responsibility for providing treatment to patients after a trial has ended does not seem likely to end soon. In September, 2003, the World Medical Association post- posed its decision about whether or not the Declaration of Helsinki should be revised to reflect concerns that the US government and the pharmaceutical industry have expressed about post-trial treatment. Paragraph 30 of the Declaration of Helsinki currently states: “At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic, and therapeutic methods identified by the study.” The proposed revision to paragraph 30 would introduce two main changes: that the physician should make every effort to see that patients receive treatment once it has been approved by appropriate authorities, and that the physician is required to explicitly tell patients if they are unlikely to continue receiving treatment from sponsors after they leave the study.

The ethical concerns over the undertaking of clinical trials in developing countries, especially with respect to the standard of treatment that should be provided to trial participants, have resulted in little research in countries where interventions are needed most. The initiation of preventative HIV vaccine trials has been delayed by debate about the provision of antiretrovirals to participants.

Thailand has been seen by many as an example of a resource-limited country that has been successful in dealing with the HIV epidemic. The Thai Ministry of Public Health began its programme to provide antiretrovirals in 1992. In 1997, about 1300 patients were receiving these drugs. Although a good start, the programme clearly did not fulfill the overwhelming need for antiretrovirals at that time.

In 1996, The HIV Netherlands Australia Thailand Research Collaboration (HIV-NAT), was formed as a non-governmental and non-profit organisation with three collaborators: the Thai Red Cross AIDS Research Centre in Thailand; the National Centre in HIV Epidemiology and Clinical Research in Sydney, Australia; and the International Antiretroviral Therapy Evaluation Centre in Amsterdam, the Netherlands. HIV-NAT’s primary aims were to undertake clinical studies of antiretrovirals and to provide access to drugs and HIV care. In the past 6 years, HIV-NAT has enrolled over 1500 participants in 20 clinical trials, and has served as an example of a clinical research institution in a resource-limited setting.

Although the current Declaration of Helsinki clearly states that every participant should be assured of treatment after the end of the trial, honouring this commitment in developing countries is difficult in practice. Until 2001, HIV-NAT has been able to procure antiretrovirals for about 300 patients after the trial, some for as long as 5 years, mainly by developing rollover protocols. This practice is increasingly difficult because there are only a small number of protocols that can be developed for highly pretreated patients. A second tactic has been to require sponsors of HIV-NAT trials to provide at least 2 years of post-trial supply either in fixed funds or in antiretrovirals. Many would say that pharmaceutical companies should provide more; however, a commitment to pay the unknown costs of life-long drug supply would considerably reduce their incentives for sponsoring trials, and, in our experience, is an assurance they are unwilling to make. Furthermore, some sponsors who are not pharmaceutical companies simply do not have funds available for post-trial care. We acknowledge that, in less developed countries, sponsors should shoulder more responsibility for long-term therapy.

In 2001, HIV-NAT recognised that almost 100 patients would soon be without further drug supplies. In a survey, most of these patients said that they would stop treatment because financial difficulties would prevent them from paying the entire amount, but almost all said they would be willing to share the cost. Although we stated clearly in our consent forms that we could not promise post-trial drug supply, we were compelled to take action when faced with the tragic prospect of watching patients reversing their excellent quality of life gained while on antiretrovirals. Therefore, the HIV-NAT drug fund was initiated in November, 2001. Because of restricted resources, a large variation in patients’ incomes, and our principle belief in shared responsibility, we based our subsidies on a co-payment and sliding scale system.

When patients apply to the HIV-NAT drug fund, the key step in the procedure is an assessment, by independent and experienced social workers, of their ability to pay. The drug fund committee, which consists of two physicians, two nurses, and a manager, reviews the social workers’ recommendation in each case, and sometimes discusses the case with the project physician and nurse who know the patient, before deciding on the amount to be subsidised. The committee might ask the project physician to consider modifying antiretroviral regimens or formulations to reduce the cost, as long as the modification does not have a deleterious effect on the patient. The support provided to patients might be in

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HIV Netherlands Australia
Thailand Research
Collaboration, Pathumwan,
Bangkok 10330, Thailand
(A. Ananworanich), N.
Cholayuth MD, T.
Teranatchalerm BN,
M. Boyce MD, K. Runyantham MD,
Prof (L. Lange MD),
Prof (D. Cooper MD),
Prof (P. Phanuphak MD)
Correspondence to: Dr Jintanat
Ananworanich
Jintanat.aj@cdsdc.ac.th
the form of cash, drugs, or both. The committee also oversees the bulk purchase of some drugs to obtain low prices. The social work team reassess the financial status of the patients every 12 months. Since we are a small organisation with five doctors and 11 nurses, some committee members might, at times, come from the patient’s study team, possibly introducing bias into the decision-making process. However, we believe that knowing the patient helps us make a more informed decision.

According to our established standard, the patient pays at least US$15 per month, and HIV-NAT pays at most US$120 per month. This sum is based in part on HIV-NAT’s 5-year financial projection. It also sets a standard for patients to meet. Like most resource-limited countries, Thailand has a wide disparity of incomes. Although many of our patients could pay US$35 per month without difficulty, we do not expect all of them to be able to, since the minimum wage in Thailand is only US$4 per day.

By October, 2003, HIV-NAT had 918 patients participating in trials and 464 who had completed trials. Of the 464 post-trial patients, 50% enrolled in new studies, 10% paid for continuing drugs themselves (with two-thirds receiving partial subsidisation from the Thai government), and 20% received drug fund support. The patients’ ability to pay was helped by the Thai government’s production of generic fixed-dose combination of stavudine, lamivudine, and nevirapine, which costs US$27 per month.

Of the 88 individuals who received drug fund support, 50 were able to pay the minimum monthly requirement of US$35 or more, 14 paid less than the this amount, and four were not able to pay anything. On average, the patient and HIV-NAT drug fund paid US$40 (range 0–206) and US$52 (2–196) per month, respectively. No patients at HIV-NAT have had to stop antiretrovirals because of lack of financial support. 15 patients needed large subsidies to fund their second-line regimens.

Income for the drug fund comes from revenues derived from research studies (overhead costs) (85%) and modest profits from other activities such as offering symposia and training courses (15%). The budget is US$47,000 for the first year and US$24,000 for subsequent years. In the past 2 years, 56% of the budget has been used. In the future, private donations might also be sought if needed. The use of funds for this purpose has not compromised HIV-NAT’s ability to undertake other HIV-related clinical research.

Within the next 2 years, we expect about 200 patients to complete their clinical trials. Most of them are on protease inhibitor-based regimens and are still benefiting from them. The present budget is sufficient to subsidise the cost of antiretrovirals for these patients, since the generic protease inhibitors to be produced by the Thai government and the long-term supply from some sponsors will help lower the price. Importantly, the Thai government is expanding its Access to Care Programme using additional funding from the Global Fund for AIDS, Tuberculosis and Malaria to provide free antiretrovirals to a larger number of patients. Even though we are fortunate that most of our patients have excellent adherence and continue to be treated effectively with their first regimens, we are concerned about providing expensive second-line regimens to a larger number of patients. We have had some success requesting grants from pharmaceutical companies to purchase their drugs and seeking funding for studies of new antiretrovirals for drug-resistant patients. In the long term, we hope to rely on inexpensive generic protease inhibitors and the Thai Government Access to Care Programme. In resource-limited settings, research institutions are invariably faced with difficulties in long-term antiretrovirals procurement. A co-payment and sliding scale drug fund programme such as ours offers organisations the option to adjust the amount of support patients receive based on their financial resources, and can be replicated in countries less developed than Thailand. Nevertheless, this is not a complete solution. For any developing country, long-term drug supply for patients at the end of a trial can only realistically be sustained if the government provides it. We hope that in the future, our HIV-NAT drug fund will be needed by only a few patients who might need antiretrovirals that are not provided by the government. A drug fund should be a temporary solution until the ultimate goal of access to all is achieved. In the meantime, allocation of institutional income for this purpose should be a priority.

Conflict of interest statement
None declared.

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